Meeting of the
Pharmacy and Therapeutics Committee
June 8, 2005

Minutes

Draft

Members Present:
Randy Axelrod, M.D., Chair
James Reinhard, M.D
Avtar Dhillon, M.D.
Roy Beveridge, M.D
Mark Oley, R.Ph.
Gill Abernathy, M.S., R.Ph.
Renita Warren, Pharm.D.

A quorum was present

Absent:
Sue Cantrell, M.D
Arthur Garson, M.D.
Christine Tully, M.D.
Mark Szalwinski, R. Ph.
Mariann Johnson, M.D.

Guests:
Manikoth Kurup, MD, Member, Board of Medical Assistance Services
45 representatives from pharmaceutical companies, providers, advocates, associations, etc.

DMAS Staff:
Jane Woods, Secretary of Health and Human Resources
Cindi B. Jones, Chief Deputy Director
Cheryl Roberts, Deputy Director of Programs and Operations
Bryan Tomlinson, Director Division of Health Care Services
Reatha Kay, Counsel to the Board, Office of the Attorney General
Keith Hayashi, R.Ph, Clinical Pharmacist
Rachel Cain, Pharm.D, Clinical Pharmacist
Katina Goodwyn, Pharmacy Contract Manager

First Health Staff:
David Adams, Pharm.D, Rebate Support
Debbie Moody, R.Ph, Clinical Manager
Donna Johnson, R.Ph, Clinical Manager
Doug Brown, R.Ph, Rebate Support
Justin Lester, Pharm.D, M.B.A ., Rebate Support

WELCOME AND INTRODUCTIONS

Dr. Randy Axelrod noted that Patrick Finnerty was away at a meeting with other State Medicaid Directors from throughout the country and would not be able to attend the meeting. Dr. Axelrod asked Secretary Woods to proceed with her comments.

COMMENTS FROM THE SECRETARY OF HEALTH AND HUMAN RESOURCES

Secretary Woods provided the welcome on behalf of Patrick Finnerty in his absence. She stated that the meeting marked the two year anniversary of the Committee and their involvement in the PDL process. She noted that what the Committee had accomplished for everyone in the Commonwealth was amazing and their willingness to share their time, expertise and energy throughout this process was appreciated by the Department as well as the Governor of this Administration and constituents throughout the Commonwealth. Secretary Woods and Patrick Finnerty have heard repeatedly in their travels throughout the country that Virginia "got it right" with the development and implementation of the Preferred Drug List. She credited the P&T Committee for the success of the PDL program as they are the true experts leading the process. Many states are looking at the Virginia models, rules and every process to bring their PDL into a similar celebratory stance. Secretary Woods extended her thanks to the entire Committee and special thanks to Dr. Axelrod, Chair, and Mark Szalwinski, Co-Chair, for their amazing leadership. The knowledge and guidance they brought to the PDL process was a "gift".

Secretary Woods stated that it is important to note that what has distinguished Virginia from other states was entrusting the PDL program to the P&T Committee and its representatives from the medical community who know exactly what to do to ensure the medical needs of recipients throughout Virginia are met. The P&T Committee was given the authority to direct decisions and this was important to make the PDL program a quality effort.

Tragically, someone who has been with the Committee throughout the whole process, Dr. Christine Tully, was not able to attend the meeting. Dr. Tully, who has been invaluable to this process, is unable to attend due to her illness. Thoughts and prayers are with Dr. Tully and everyone involved looks forward to the day when she is feeling strong enough to return. In Dr. Tully's absence, the Secretary stated that she is grateful to Dr. Peter Boling, MCV's Director of Geriatric Services, who has ensured that he would provide expertise from his department. As a result, Dr. Rachel Selby-Penczak attended the meeting to provide commentary. She would not be voting because the Committee did not provide for proxy voting; however, she would share her expertise with the committee. The Secretary thanked Dr. Selby-Penczak for attending the meeting.

The Secretary provided an update regarding the recent activity throughout the country in dealing with Viagra and other drugs that treat erectile dysfunction (ED). She stated that it was probably one of the very few times where Virginia's very rigid, narrow, cost saving eligibility for Medicaid has probably kept Virginia from being in the same position that other states found themselves; where they had hundreds of people on their Sex Offender Registry receiving ED drugs through the Medicaid Program. Virginia did discover 52 Medicaid recipients who were on the registry and also receiving ED drugs. The Governor issued an emergency order and the Department took emergency action to address this issue. The Department moved forward with emergency regulations so the offenders on this registry will not have access to ED drugs within hours of the emergency order by the Governor. The Governor has further directed the Secretary to bring together some expertise in this area. The Secretary stated that she may be calling upon many of the P&T Committee members if there is anything else to be done in terms of Medicaid providing these ED drugs to other recipients such as sex offenders who have served their time and are no longer in prison, but whose crimes did not rank of a nature to put them on the registry. The Department will have to decide if this is a medically appropriate drug that requires access. The Secretary noted that she realizes these drugs have other uses and the use of the drug for Pulmonary Arterial Hypertension was recently approved; therefore, the Department does not want to eliminate ED drugs immediately or completely. This issue continues to be reviewed.

The Secretary announced that the Department has moved forward with an exciting program in conjunction with the Department of Mental Health, Mental Retardation, and Substance Abuse Services. These agencies are working collaboratively to address issues of outlier prescribing in the arena of behavioral health medications. She stated that the agencies are utilizing the Behavioral Pharmacy Management System (BPMS) a program administered by Comprehensive NeuroScience (CNS) and supported by Lilly. Letters to providers to introduce the program were distributed in April. Physicians will conduct peer-to-peer reviews regarding outlier prescribing patterns to ensure that recipients are receiving the best possible, best practice and most effective medical interventions. The first set of intervention letters will be mailed by the end of June 2005. This is a quality initiative as opposed to having costs drive good medical decisions. The Secretary stated that Virginia is certainly, even now not quite at the end of this Administration, better able to say we are being very good stewards of tax payers dollars and are also being very responsible in ensuring the health and wellness of our Medicaid lives.

COMMENTS FROM THE CHAIRPERSON

Dr. Axelrod thanked everyone for working hard at the previous meeting, which he could not attend. He requested a presentation on the consequences of Medicare Part D at the next P&T Committee meeting. He referenced a letter from CMS to DMAS that directed what Medicaid would have to cover post Medicare Part D. He believes an overview of these coverage requirements will help the Committee better understand the changes that will be occurring in January 2006. The Department agreed to prepare a presentation of Medicare Part D information for an upcoming P&T Committee meeting.

ACCEPTANCE OF MINUTES FROM March 23, 2005 MEETING

Dr. Axelrod asked if there were any corrections, additions, or deletions to the minutes from the March 23rd meeting. None were noted, and upon request of the Chairman, the Committee voted on a motion and a second to approve the minutes of the March 23rd meeting as written. The Committee voted to approve the minutes as drafted.

Review of New Drugs in PDL Classes/ Drug Class Discussions

Dr. Axelrod stated that the meeting will include the quarterly review of new drugs in existing PDL drug classes. He stated that there would be presentations on these drugs and Mark Oley would summarize clinical information regarding the new drugs. The meeting would also include a confidential meeting to discuss the PDL classes and discussion would be completed in the public meeting. For everyone new to the meeting format, Dr. Axelrod reviewed the rules of the time clock; each speaker was allowed three minutes to present excluding any questions posed by the Committee.

Melissa Longstreet Kay; -Sepracor, Inc. discussed Lunesta®, a Sedative Hypnotic

Lunesta® is a new non benzodiazepines sedative hypnotic agent that was approved by the FDA on December 15, 2004 and was launched on April 4, 2005. Lunesta® is available in three doses, e.g., 1 mg, 2 mg, 3 mg tablets. Lunesta® is indicated for the treatment of insomnia. In controlled outpatient and sleep laboratories studies, Lunesta® administered at bedtime decreased sleep latencies or onset of sleep and improved sleep maintenances or sleep throughout the night. Ms. Kay cited studies on the effect of Lunesta® on reducing sleep latencies and improving sleep maintenances. From these studies she cited that Lunesta® has been shown to help patients fall asleep and stay asleep with little to no side effects and that it is more effective than placebo. It is well tolerated and the biggest side effect is an unpleasant taste.

Paul M. Spector, D.O. discussed Lunesta® a Sedative Hypnotic

Dr. Spector noted that he was not an employee of Sepracor and he is not on the speakers list for Sepracor. He has no financial connection with the company. Dr. Spector stated he was attending to ask that Lunesta® be added to the formulary list on equal basis with Ambien® and Sonata®. Lunesta® is extremely effective in sleep maintenances and sleep onset, it is the only non benzodiazepines in the class that address sleep maintenances and is indicated for long-term use. The other drugs on formulary that are alternatives are not for long term use. The other drugs are effective for up to 14 days only as is documented by the Food and Drug administration (FDA) and Physician Desk Reference (PDR). Trazodone® is not approved for sleep by the FDA. Trazodone® has a half life between 6.5 and 11 hours and 11 hours in the elderly. With newer drugs called the Z drugs, zolpidem (Ambien®), zaleplon (Sonata®) and eszopiclone (Lunesta®), they all have much shorter half lives. The half life and the duration of action are not necessarily the same. Though often times there are problems with drugs with long half lives because they have long durations of action, Lunesta®'s duration is about an hour longer than its half life. It does not produce residual sleepiness the next day and there is only one night of rebound the next night. Lunesta® is a sedative hypnotic, schedule IV molecule indicated for sleep onset and sleep maintenance. In summary, Lunesta® is approved for long-term use. No development of tolerance to any sleep parameter has been noted in long-term studies. There is a low potential for abuse. No significant rebound insomnia at doses up to 3mg. No next day residual effects noted in clinical trials and it is non-narcotic. No clinically relevant drug – drug interactions with warfarin or lorazepam.

Mark Oley asked if the reason for little residual sleep effect was because of the 6 hour half life of Lunesta®.

Dr. Spector stated that was correct. The drug does not cause the residual sleepiness and stupor that some people experience. People feel better in the morning, more refreshed. Some do have residual sleepiness which may only last for a half hour.

Dr. Beveridge asked Dr. Spector to clarify if he was saying that there is some clinical difference between these drugs.

Dr. Spector replied that he does not want to criticize other drugs but Trazodone® is not approved for sleep.

Dr. Axelrod asked Dr. Rachel Selby-Penczak if she had a comment.

Dr. Rachel Selby-Penczak replied that she had never used Lunesta® but in the elderly she often uses Trazodone®.

Dr. Spector stated that one of the problems with Trazodone® is the cardiac arrhythmia in the elderly.

Mark Oley reviewed Lunesta® for the Sedative Hypnotic class

Lunesta® is a new sedative hypnotic that is a new class called the pyrrolopyrazine derivative. It has no structural similarity to zolpidem, zaleplon or the benzodiazepines. All of these drugs are believed to act through the GABA A subtypes. The drug's exact mechanism of action in enhancing sleep is unknown. It is available as 1 mg, 2 mg, and 3 mg tablets. The recommended starting dose is 2 mg at bedtime, which can be increased to 3 mg. The real difference between Lunesta® and other sedative hypnotics is that long term studies were performed so that the duration of therapy is not restricted to 12 weeks.

Mark Oley made a motion to make Lunesta® PDL eligible.

This motion was seconded and unanimously approved by the Committee

Fran E. Kaiser, MD, AGSF, FGSA Executive Medical Director, Regional Medical Director Merck & Company discussed Fosamax plus D® a Bisphosphonate for Osteoporosis

Dr. Kaiser stated that Fosamax plus D® reduces the rate of fractures of the hip and spine. The components of Fosamax plus D® are 70 mg of alendronate and 2800U Vitamin D in a single tablet that is taken weekly. Vitamin D plays a critical roll in both bone health as well as muscle skeletal function. Vitamin D maintains serum calcium in the normal range. Only now is the role Vitamin D plays recognized in maintaining muscle skeletal function. Low vitamin D can lead to muscle weakness and bone loss. There is a window in which Parathyroid hormone (PTH) and Vitamin D seem to coexist peacefully. Dr. Kaiser reviewed various studies. One cited that 52% of women had low Vitamin D levels and patients with fractures had low Vitamin D levels. He cited a conclusion from this information is that the combination of alendronate and Vitamin D would improve Vitamin D levels and lead to less fractures.

Christina Israel, PharmD, FCCP, BCPS; Regional Manager, Primary Care Scientific Field Operations, Medical Affairs for Roche Laboratories discussed Boniva® a Bisphosphonate for Osteoporosis

Dr. Israel reviewed the BONE TRIAL which was a 3-year vertebral fracture study required by the FDA for approval of an osteoporosis therapy. She discussed the results of the trial. Relative risk of vertebral fractures was reduced by 52% in this trial. Vertebral fractures are the accepted measure of osteoporotic fractures for registration trials as they occur spontaneously in the normal course of a disease. The BONE study was not designed or powered to test difference in non-vertebral fractures, as these fractures require trauma and make it difficult to control in a study. The incidence of clinical non-vertebral fractures was low in all groups. However, a post hoc analysis in higher risk patients (femoral neck BMD T-score <-3; N=375) produced a 69% relative risk reduction in non-vertebral fractures compared to placebo.

Significant and progressive increases in bone mineral density (BMD) were observed at the lumbar spine (6.5%) and at all hip sites [total hip (3.4%); femoral neck (2.8%) trochanter (5.5%)] in the 2.5 mg daily group compared to baseline. Substantial reductions of uCTX (marker of bone resorption) were observed by 3 months and sustained throughout the 3-year study period (median decrease 65%). Newly formed bone induced by long- term treatment of BONIVA® was found to be of normal quality. With regard to safety, the overall adverse event profile of ibandronate (BONIVA®) was similar to that of placebo. She then reviewed the MOBILE TRIAL (Non-inferiority trial comparing 150 mg monthly ibandronate vs. 2.5 mg daily on LS BMD) which was the FDA accepted methodology for approving extended dosing intervals of bisphosphonates. LS BMD gains are compared between the extended dosing regimen and the daily dosing regimen with proven anti-fracture efficacy. Lastly she reviewed recommendations from the surgeon general to simplify treatment regimens to increase compliance and adherence with osteoporosis agents. Her final points were that Ibandronate 150 mg monthly is the first approved monthly treatment for any disease. Ibandronate is approved for prevention and treatment of postmenopausal osteoporosis. Simplified dosing regimens have the potential to increase compliance and persistence with osteoporosis therapy. BONIVA® has a robust vertebral fracture reduction with good tolerability and safety profile.

Mark Oley reviewed the new Bisphosphonates for Osteoporosis

Fosamax® plus D and Boniva® both are new Bisphosphonates released in the past quarter for Osteoporosis. Fosamax® plus D is what the name implies - a combination of Fosamax® 70mg and Vitamin D 2800U in a single tablet. It is made by Merck. Boniva® (ibandronate) is made by Hoffman-La Roche partnered with GlaxoSmithKline. It is has a once-daily formulation already approved. The launch of the drug was held pending the approval of the extended-release once-monthly oral formulation. This became available May 2005. There are still no head-to-head clinical trials of alendronate (Fosamax®) versus risedronate (Actonel™) versus Ibandronate (Boniva®).

Mark Oley made a motion to make Fosamax® plus D and Boniva® PDL eligible.

This motion was seconded and unanimously approved by the Committee

Mark Oley reviewed Itraconazole for the Onychomycosis Antifungals class

Itraconazole is a newly released generic for the established brand drug Sporanox®.
No new or different information.

Mark Oley reviewed Felodipine for the Calcium Channel Blockers class

Felodipine is a newly released generic for the established brand drug Plendil®.
No new or different information.

Mark Oley reviewed Prevacid NapraPAC® for the Analgesic- NSAIDs class

Prevacid NapraPAC® is a combination drug of Prevacid 15 mg a proton pump inhibitor (PPI) and Naproxen in either 375 or 500 mg (a NSAID). It is being reviewed for consideration as an NSAID.

Mark Oley made a motion to make all three drugs reviewed, Prevacid NapraPAC®, Itraconazole, and Felodipine PDL eligible.

This motion was seconded and unanimously approved by the Committee.

Dr. Axelrod noted that the committee needed to review financial information on these drugs and asked the Attorney General office for guidance.

Comments from the Office of the Attorney General

Ms. Reatha Kay from the Attorney General's office stated that under the Virginia Freedom of Information Act (FOIA), specifically Virginia Code section 2.2-3711, a public body such as the P&T Committee, may

go into a closed session for any of the 33 reasons listed in that statute. The discussion of manufacturer and wholesaler prices is not one of the 33 reasons listed.

She stated the Attorney General strongly supports the principles of open government embodied by the FOIA and believes in the opportunity of the Commonwealth's citizens to witness the operation of government to the fullest extent.

Federal Law 42 U.S.C. 1396r-8(b)(3)(D) requires such pricing information to be kept confidential. On this point, federal law supersedes the Virginia FOIA. Since the P&T Committee must discuss this pricing information as part of its duties, pursuant to federal law, a confidential meeting must occur for the consideration of this pricing information. She cautioned, only this confidential information should be discussed.

Mark Oley made a motion for the P&T Committee to resume the meeting in another room to discuss this confidential information regarding prices charged by the manufacturers and wholesalers of the drugs discussed at this P&T Committee meeting. This confidential meeting is authorized by Federal Law at 42 U.S.C. § 1396r-8(b) (3) (D) that requires this information to be kept confidential.

This motion was seconded and unanimously approved by the Committee.

The meeting adjourned to an executive session.

The Committee returned to the public meeting and a motion was made to resume the meeting. The motion was seconded and unanimously approved by the Committee.

Mark Oley noted that to the best of each member's knowledge only such matters required to be confidential under federal law Federal Law at 42 U.S.C. § 1396r-8(b) (3) (D) were discussed.

Dr. Axelrod reviewed the definition of "PDL eligible" for the group. "PDL eligible" is defined, for purposes of the P&T Committee, as drugs within their class with comparable clinical qualities; therefore, they may be considered equally from a financial perspective. There are some exceptions in which there are specific drugs that must be included on the PDL, based on their clinical superiority, labeling, etc., which makes it a "must have" within the PDL eligible drug class. Once new drugs are designated "PDL eligible", the next step is to review each of the drugs under consideration for inclusion or exclusion on the PDL (preferred/ non-preferred) from a financial sense in confidential session. Dr. Axelrod also noted each drug class is reviewed with its appropriate PDL phase and in the fall a re-review of all phase one drugs will be done. If a new drug was reviewed at this meeting and is in phase one drug class, it will be reconsidered globally with other drugs included in phase one in the fall when both clinical and financial information will be reviewed.

Mark Oley motioned that in the Bisphosphonates for Osteoporosis class the following products be considered preferred:
Actonel®
Fosamax®
Fosamax® Solution
Fosamax plus D®

This motion was seconded and unanimously approved by the Committee.

Mark Oley motioned that in regards to the Sedative Hypnotics class that the current PDL be status quo; the current PDL would continue without change.

This motion was seconded and unanimously approved by the Committee.

Mark Oley motioned that in regards to the Analgesic- NSAIDs that the current PDL be status quo with the current PDL continued without change.

This motion was seconded and unanimously approved by the Committee.

Dr. Axelrod reminded the group that PDL "preferred" means if you prescribe the drug it is dispensed. If it is a "non-preferred" drug, then the prior authorization process is required as administered by the First Health Services call center. Being designated as "non-preferred" does not mean the drug is not accessible.

Mark Oley motioned that in regards to the Calcium Channel Blockers, the generic (Felodipine) be PDL preferred.

This motion was seconded and unanimously approved by the Committee.

Mark Oley motioned that in regards to the Onychomycosis Antifungals, the generic (Itraconazole) be PDL preferred.

After discussion, this motion was amended to designate Itraconazole as non-preferred.

The amended motion was seconded and unanimously approved by the Committee to designate Itraconazole as non-preferred.

Review of New Drug Classes for PDL Eligibility

Geraldine Anastasio, Pharm D, BCPS, Director, Regional Medical Research Specialist, Urology/Sexual Medicine for Pfizer, discussed Detrol® a Urinary Tract Antispasmodic

Detrol® is the most prescribed urinary incontinence product of all agents in its class by both urologists and primary care physicians. It is the first prescribed because it is considered the safest and has the best tolerability profile. Drugs that have difficult side effects decrease compliance in patients. She reviewed two studies. The Freeman study showed a 6-fold increase in the population who were able to complete a task. This was considered to be meaningful to the people completing the study. The second study was the Athenopolis study which showed that men could benefit from Detrol®. It was safe and effective with no residual flow. Detrol® is a non-selective antimuscarinic receptor blocker; it affects both the M2 and M3 receptors. This is important because it created a balanced non selective mechanism of action. Detrol® is a short-acting product with a once-daily dosage form. One of the benefits is that if the geriatric patient has a problem then the drug is out of their system in 24 hours. This is the most tolerated and prescribed product on the market.

Gill Abernathy asked about the M3 being the receptor for the pathogenic bladder.

Dr. Anastasio noted that the old, ischemic tissue was thought to be responsible for the overactive bladder (OAB) and this is the pathologic bladder.

Dr. David Glazier, Co-Director, Virginia Urology Continence Center, discussed Detrol LA® a Urinary Tract Antispasmodic

Dr. Glazier is the chairman of the research section of Virginia Urology. They run multiple clinical trials, conduct much consulting, and they do work with Pfizer. He is part of a large practice that sees both male and female patients. The group sees a large range of patients with multiple disease states. He reviewed the concerns his patients faced with regard to compliance with drugs that have to be dosed three to four times a day. He supports inclusion of Detrol LA® because of once a day dosing. Dr. Glazier reviewed the LANDES trial that evaluated Detrol LA® over 6 months. Noted was a significant reduction in symptoms.

He also reviewed the OPERA study of 2003 that evaluated Ditropan XL® versus Detrol LA®. It showed equal efficacy between the two products but Detrol LA® had much less side effect of dry mouth.
Dr. Glazier requested Detrol LA® be preferred PDL drug.

Gill Abernathy asked about the OPERA trial and if the trial failed to show a difference in efficacy.

Dr. Glazier replied, no, it showed the two drugs were equal in efficacy; the difference was the difference in side effects.

Mark Oley asked if the side effect dry mouth was dose dependent for all agents.

Dr. Glazier replied yes, that it is dose dependent.

Lori Helke, RPh, FASCP, CGP, Clinical Manager for NeighborCare Pharmacies, discussed Detrol LA® a Urinary Tract Antispasmodic

Ms. Helke attended as an advocate for the geriatric patients with whom she consults. She asked that Detrol LA® to remain unrestricted for Medicaid patients. As support for her request, she cited the Beers list which addresses the antispasmodic and anticholinergic side effects. Detrol LA® has fewer side effects and has a more positive risk-versus benefit profile than other drugs within its class. One of Ms. Helke's goals, in her work, is to help her population maintain a high quality of life, to reduce possible falls, allow them to stay at home a little while longer and avoid Long Term Care intuitions as long as possible.

Stephen B. Camper, PhD, Scientific Liaison, Astellas Pharma US, Inc., discussed VESIcare® a Urinary Tract Antispasmodic

The definition of overactive bladder (OAB) as approved by the Standardization Subcommittee of the International Continence Society (ICS) in September 2001 is defined as urgency, with or without incontinence, usually with frequency and nocturia. The purpose of the NOBLE project was to develop a research definition of OAB, estimate its overall prevalence and the burden of illness, and to differentiate between OAB populations (i.e., wet vs. dry patients). Based on survey results, the overall prevalence of OAB was 16.9% in women and 16.2% in men, with an increase in OAB symptoms with advancing age. The NOBLE study indicated that the prevalence of OAB was 30.6% in patients 65 to 74 years of age and 32.6% in patients' $\geq$ 75 years of age. Based on extrapolation of the reported prevalence rates, 33.3 million adults in the United States have OAB, with 12.2 million and 21.2 million having incontinence and being incontinent, respectively. Solifenacin (*VESIcare®*) is a competitive muscarinic receptor antagonist. Muscarinic receptors play an important role in several major cholinergically mediated functions, including contractions of urinary bladder smooth muscle and stimulation of salivary secretion. *VESIcare®* is well absorbed and extensively metabolized by the liver and has an extended elimination half-life ($t_{1/2}$) of approximately 50 hours (45 to 68 hours) resulting from its extensive distribution and slow elimination, which permits once-daily dosing. Steady state plasma levels were attained after approximately 10 days of once-daily dosing. No dosage adjustment based on patient age is required. The pharmacokinetics of *VESIcare®* is not significantly influenced by gender.

Mark Oley asked if there is any effect on cardiovascular systems from the class in general.

Dr. Camper replied no, there are no significant cardiovascular side effects. However, with the newer products they are being evaluated for QT prolongation. To date this has not been an issue.

Christopher Barnowski, MD, Medical Science Liaison, Ortho-Urology, Ortho-McNeil Pharmaceutical, Inc. , discussed Ditropan XL® a Urinary Tract Antispasmodic

Ditropan XL® is a non-selective antimuscurinic agent used for the treatment of overactive bladder with symptoms of urge urinary incontinence, urgency and frequency. He focused on two main points - efficacy and safety. Looking at efficacy the OPERA trial was a head to head trial that showed Ditropan XL ® to be superior. The primary outcomes in both groups were not significantly different. The Ditropan

XL® was dosed on the lower end of the dose spectrum. In terms of safety, both groups showed similar side effects. 93% of Ditropan XL® patients and 95% Detrol LA® patients did not experience dry mouth that would be considered clinically significant (Opera). CNS effects (dizziness, somnolence, depression and confusion) are rare and similar in magnitude between Ditropan XL® 10mg and Detrol LA® 4mg (OPERA). An expert panel of gerontologists reached consensus that Ditropan XL® is considered safe for use in the elderly – specifically excluded XL from Beers List 2003 revision.

Ray E. Lancaster, Pharm. D, Regional Account Scientific Associate Director, Novartis Pharmaceuticals Corp., discussed Enablex®(darifenacin) a Urinary Tract Antispasmodic

Enablex® was developed by Pfizer. It is a potent M3 selective inhibitor and is hepatically metabolized. Efficacy is not the issue here; it is safety. Two trials have shown safety with Enablex®; no QTC prolongation has been seen even at high doses. In a trial with Bentyl® compared with Enablex®, no cognitive impairment was seen with Enablex®

Mark Oley reviewed the Urinary Antispasmodics class

There are currently 5 FDA approved Urinary Antispasmodics. All of the Urinary Antispasmodics are FDA approved for treatment of urge urinary incontinence, frequency and urgency. Oxybutynin is available as a tablet, syrup, two to four times daily dosing; extended release tablet once a day dosage; and a patch for topical administration twice a week dosing. Tolterodine is available as a tablet twice a day dosage and an extended release capsule once daily dosage. Trospium is available as an extended-release tablet twice a day dosage. Solifenacin is available as an extended-release tablet once daily dosage. Darifenacin as an extended-release tablet once daily dosage. They all have comparative efficacy. Immediate release formulations of oxybutynin and tolterodine found no differences in efficacy.

Immediate release products to the corresponding extended release product found no differences in efficacy. Mixed results were observed with comparisons of the two extended release products – the better study (as determined by OHSU criteria) found the products equal.

The transdermal formulation of oxybutynin was compared to oxybutynin immediate-release and tolterodine extended-release and no differences in efficacy measures were observed.

Evidence from short-term head-to-head comparison trials indicate a higher incidence of adverse events overall, and dry mouth specifically with oxybutynin. The extended-release forms of each drug resulted in fewer adverse events, and dry mouth when compared to the immediate release formulations.

The comparison of transdermal oxybutynin to tolterodine extended release found a significant difference favoring the tolterodine in the withdrawal rate due to adverse events (largely due to application site reactions).

Trospium is administered twice a day which is a disadvantage for the new drug when compared with the extended-release formulations of oxybutynin and tolterodine, which are administered once a day, and the transdermal formulation of oxybutynin (Oxytrol®), which is administered twice a week.

Mark Oley motioned that all Urinary Antispasmodics be made PDL eligible.

Dr. Spector stated that an extended release formulation would be needed on the PDL.

The motion that all Urinary Antispasmodics be made PDL eligible was seconded and unanimously approved by the Committee.

Jennifer Zarintash, D.O., Medical Science Liaison, First Horizon Pharmaceutical Corp discussed *Triglide*™ a Lipotropic Non-Statin: Fibric Acid

Triglide™ (fenofibrate) is being launched in July of 2005. It is a new unique delivery system called Insoluble Drug Delivery® system; it consists of a microparticles technology (IDD®-P). Its bioavailability is not affected by food. With a high fat or low fat meal, the absorption is the same. The safety and efficacy is the same as with the previous formulations of fenofibrate. It is made in a 50 mg and 160 mg tablet. It is used to treat primary hypercholesterolemia.

Dr. Axelrod asked if an approved PI was being sent. Dr. Zarintash agreed to send the PI and dossier when available.

Mark Oley reviewed Lipotropics Non-Statins: Fibric Acid

All three of the fibric acid derivatives are FDA approved for treatment of hypertriglyceridemia and hypercholesterolemia. There are two generic names and four brand names: *Gemfibrozil* Lopid® Tablets: 600 mg Twice daily, *Fenofibrate*: Tricor®, Antara® , and now Triglide™ Tricor® Tablets: 48 mg, 145 mg -- a new formulation approved November 5, 2004, which can be taken with or without food. The original formulation had to be taken with food to maximize absorption. *Note:* Plasma concentrations of fenofibric acid after administration of three 48 mg or one 145 mg tablets are equivalent under fed conditions to one 200 mg capsule Once daily. Antara® Capsules: 43 mg, 87 mg, 130 mg should be taken with meals once daily. Triglide™ will come in 50mg and 160mg tablets, which can be taken with or with our food.

Mark Oley motioned that all Lipotropics Non-Statins: Fibric Acid is made PDL eligible.

The motion was seconded and unanimously approved by the Committee as PDL eligible.

Mark Oley reviewed Lipotropics Non-Statins: Niacin Derivatives

Currently there are 6 Niacin Derivatives; all are FDA approved for the treatment of hypertriglyceridemia and hypercholesterolemia. They are Niacin sustained release, Niaspan®, Nicobid®, Nicobid® tempules, Nicotinex®, and Slo-niacin®. Dosing is as follows: oral, immediate release, initial 100 mg 3 times/day, increase to 1 g 3 times/day, max 6 g/day, oral, extended release, initial, 500 mg at bedtime for 4 wk, then 1000 mg at bedtime for 4 wk; titrate by tolerability and efficacy; max 2000 mg/day. The efficacy and side effect profiles between the products are comparable. The side effect of flushing is generally less bothersome in the sustained release formulations. This is a class effect.

Mark Oley motioned that all six of the Lipotropics Non-Statins: Niacin is made PDL eligible.

The motion was seconded and unanimously approved by the Committee as PDL eligible.

Mark Oley reviewed Electrolyte Depleters

There are three available agents in this category, none of which are available as a generic. In addition to the prescription products available, calcium carbonate products such as Tums® or aluminum and magnesium products have also been used as phosphate binding agents.

For patients with chronic kidney disease with kidney failure (stage 3-4), calcium-based phosphate binders are effective in lowering serum phosphorus levels (EVIDENCE clinical trial) and may be used as the initial binder therapy (OPINION clinical trial).

The available evidence supports that all of the current phosphate binders are efficacious in controlling serum phosphorus levels. The products are Renagel® (sevelamer HCl) Tablets 400mg & 800mg; PhosLo® (calcium acetate) Tablets 667mg and Fosrenol® (lanthanum carbonate) Tablets 250mg & 500mg.

Mark Oley motioned that all six of the Electrolyte Depleters be made PDL eligible.

The motion was seconded and unanimously approved by the Committee as PDL eligible.

Mark Oley reviewed Topical Immunomodulators

There are currently 2 topical immunomodulators available in the United States. Both are FDA approved for treatment of atopic dermatitis. Both products are indicated for short-term and intermittent long-term treatment of atopic dermatitis only. Long term or continuous use is not approved. Both products received an indication for second line therapy. Elidel® is currently available only as a cream; Protopic® is currently available only as an ointment.
Elidel® is indicated for non-immunocompromised patients. Protopic® does not contain language in its indication about immunocompromised patients. Elidel® and Protopic® 0.03% are indicated in patients 2 years old and older. Protopic® 0.1% is indicated in adults only. The FDA issued a public health advisory to inform healthcare providers and patients about a potential cancer risk from use of Elidel® (pimecrolimus) and Protopic® (tacrolimus), products that are applied to the skin. This concern is based on information from animal studies, case reports in a small number of patients, and how these drugs work. It may take human studies of ten years or longer to determine if use of Elidel® or Protopic® is linked to cancer. In the meantime, this risk is uncertain and FDA advises that Elidel® and Protopic® should be used only as labeled, for patients who have failed treatment with other therapies. The FDA recommends that healthcare providers, patients and caregivers consider using Elidel® and Protopic® only as second-line agents for short-term and intermittent treatment of atopic dermatitis (eczema) in patients unresponsive to, or intolerant of other treatments and to avoid use in children younger than two years of age. Elidel® cream and Protopic® ointment are topical immunosuppressant calcineurin inhibitors that are applied to the skin and are the only approved drug products in this class.

Mark Oley motioned that both Topical Immunomodulators be made PDL eligible.

The motion was seconded and unanimously approved by the Committee as PDL eligible.

Mark Oley reviewed Immunomodulators for Rheumatoid arthritis (RA).

In rheumatoid arthritis (RA) the goals of treatment are to slow the progression of the disease and to provide relief of symptoms, thereby improving quality of life. There are currently two types of biologic immunomodulators. The tumor necrosis factor (TNF) blockers, etanercept and adalimumab, act by binding to TNF, thereby blocking its interaction with receptors. Anakinra, an interleukin-1 (IL-1) receptor antagonist, creates inhibition by binding to IL-1 receptors. All three agents have been proven safe and effective in treating RA. In addition, etanercept has received FDA approval for treating polyarticular-course juvenile RA, psoriatic arthritis, ankylosing spondylitis and plaque psoriasis. Unfortunately, good head-to-head comparisons are lacking in this drug category. Individual patients differ in the course of disease, its signs and symptoms, and its effect on quality of life. Therefore, treatment of immune mediated inflammatory disease needs to be tailored to the individual patient. The monitoring of individual response should not be based solely on ACR response criteria, but should rely on more subjective measures as well. The drugs included in this class are Enbrel®, Humira®, and Kineret.

Dr. Axelrod asked if the Committee was considering this class for RA only or if we are also considering other indications. Mark Oley stated that at this time only indications for RA were being considered.
Dr. Axelrod expressed the complicated nature of this class and the rapid expansion of the category for other indications. Dr. Axelrod also cautioned that this drug class would also cross Medicare and Medicaid coverage requirements. He also noted that with this class there are extraordinary clinical considerations and several drugs in the pipeline. This is the first drug class being reviewed by the P&T Committee in the area of "biologicals" or specialty drugs which involve large expenditures.

Mark Oley motioned that the Immunomodulators be made PDL eligible.

Dr. Beveridge expressed the issue that this is a very complicated class. It was requested by the Committee that additional clinical information be presented at the next meeting. Dr. Axelrod requested additional presentations, further discussion of this class, and consideration special clinical criteria.

The motion was seconded and unanimously approved by the Committee as PDL eligible

Philip Swartz, Medical Science Liaison, Serono, Inc. discussed Multiple Sclerosis Agents

Two thirds of the people with MS are female between the ages of 25 and 35. There are 4 FDA approved drugs. Three are interferons. Rebif® is currently the number one interferon. Rebif® is the first drug and only drug to overturn the orphan drug status of Avonex® by the FDA. There are very few if no head to head studies within this class. Rebif® has the largest amount of clinical experiences of any of the MS drugs. Rebif® is the only drug to affect all three parameters of MS.

Mark Oley reviewed Multiple Sclerosis Agents

There are three interferon betas available for the treatment of MS: Interferon beta 1-b (Betaseron®), interferon beta 1-a (Avonex®) and interferon beta 1-a (Rebif®). Even though the latter two agents are both interferon beta-1a, it is possible that minor differences exist and that they may not be equivalent.

Each of these agents have proven to be effective vs. placebo. However, there are limited comprehensive 'head to head' trials available in this class. Those that are available are limited in their usefulness due to their study design or because of differences in measuring and defining outcomes. Dosing of these drugs are, Betaseron® SQ injection every other day, Avonex® IM injection once a week, and Rebif® SQ injection three times a week.

Mark Oley suggested that further clinical information also be provided for this class as it is also a specialty drug class with unique considerations based on clinical significance and step therapy guidelines. Dr. Axelrod recommended that clinical experts (rheumatologists for immunomodulators and neurologists for multiple sclerosis drugs) be available at the next meeting to discuss more clinical information with the specialty drug classes.

Mark Oley motioned that the Multiple Sclerosis Agents be made PDL eligible.

The motion was seconded and unanimously approved by the Committee as PDL eligible with the notation that an expert panel will provide further clinical information for consideration in the future.

Open Issue Reviewed by Cindi B. Jones, DMAS Chief Deputy Director

Ms. Jones reviewed the status of COX 2 drug class. She stated that there continues to be market changes related to the COX 2 drug class. Following the market withdrawal of Vioxx® in September 2004, the drug Bextra® was voluntarily withdrawn from the market in April 2005. Prior to this announcement, Bextra® was a non-preferred drug in the Cox-2 drug class on the PDL and required prior authorization for coverage. Effective April 7th, prior authorizations are no longer granted for Bextra® and it is not reimbursable by Virginia Medicaid. A mailing was distributed to both medical providers and recipients with recent Bextra® claims to notify them of this change. The only preferred drug in the COX-2 class is Celebrex®, which continues to be reimbursed without prior authorization. The clinical edit is currently still in place requiring patients under age 60 to try two Non-steroidal Anti-Inflammatory Drugs (NSAIDs) or have been identified with a designated co-morbid condition prior to approval of a Cox-2 drug. These NSAIDs are covered in both prescription-strength and over the counter.

With the implementation of the COX-2 drug class on the PDL in July 2004 and under the direction of this Committee, the Department allowed patients under age 60 who were on COX-2 therapy between January and June 2004 to receive a one-year prior authorization to bypass both the clinical and PDL edits related to this class. All unexpired prior authorizations for these particular patients will terminate on June 30,

2005. After this date, these patients will need to receive a new prior authorization for the clinical edit to receive the preferred drug, Celebrex®. The recent mailing to medical providers also addressed the termination of these prior authorizations.

In addition, the P&T Committee allowed an exemption from the COX-2 clinical edit (step therapy) for recipients for over age 60. This exemption for the over 60 population will also expire on June 30, 2005; requiring all recipients to receive prior authorization based on the clinical edit. Information on the end of this exemption will be posted to the DMAS web site and long term care pharmacy providers will also receive notification.

Dr. Axelrod asked if there were any other comments, thoughts, or questions to come before the Committee. There were none. Dr. Axelrod expressed his appreciation for another great meeting and to the Committee for their time.

The next meeting date is to be determined. The Chairman adjourned the meeting.